

*AR* wherein thiophene is the only heterocyclic substituent.

No new matter has been introduced.

REMARKS

Claims 1 and 6 are amended herewith to include the limitation that the compounds according to these claims contain thiophene as their only heterocyclic substituent, in accordance to the Restriction Requirement (Paper No. 4) issued May 5, 1999, in parent application 09/159,335 (see, e.g., Group V).

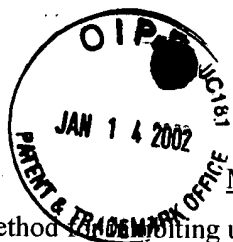
It is believed that in view of Applicants' foregoing amendments to the claims, the pending claims are now in condition for allowance. A favorable action is earnestly solicited. If the Examiner would like to discuss any of the issues raised in the Preliminary Amendment, Applicants' Representative can be reached at 617-720-3500 x286.

Respectfully submitted,

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MARKED-UP CLAIMS

1. (Amended) A method of inhibiting unwanted cellular proliferation associated with an inflammatory disease, said method comprising the step of contacting a cell the proliferation of which contributes to inflammation *in situ* with an effective amount of  
a compound having the formula:



or a pharmaceutically acceptable salt or hydrate thereof, wherein:

n is 0, 1, 2, 3 or 4;

X is absent, (C<sub>1</sub>-C<sub>3</sub>) alkyl, (C<sub>1</sub>-C<sub>3</sub>) alkenyl, or (C<sub>1</sub>-C<sub>3</sub>) alkynyl;

Y is C, N, P, Si or Ge;

R<sub>1</sub> is absent, -halo, -R, -OR, -SR, -NR<sub>2</sub>, -ONR<sub>2</sub>, -NO<sub>2</sub>, -CN, -C(O)R, -C(S)R, -C(O)OR, -C(S)OR, -C(O)SR, -C(S)SR, -C(O)NR<sub>2</sub>, -C(S)NR<sub>2</sub>, -C(O)NR(OR), -C(S)NR(OR), -C(O)NR(SR), -C(S)NR(SR), -CH(CN)<sub>2</sub>, -CH[C(O)R]<sub>2</sub>, -CH[C(S)R]<sub>2</sub>, -CH[C(O)OR]<sub>2</sub>, -CH[C(S)OR]<sub>2</sub>, -CH[C(O)SR]<sub>2</sub>, -CH[C(S)SR]<sub>2</sub> or aryl;

Ar<sub>1</sub> is aryl, substituted aryl, heteroaryl other than imidazole, nitroimidazole and triazole, heteroarylium other than imidazolium, nitroimidazolium and triazolium, (C<sub>5</sub>-C<sub>8</sub>) cycloalkyl or (C<sub>5</sub>-C<sub>8</sub>) heterocycloalkyl;

Ar<sub>2</sub> is aryl or substituted aryl;

Ar<sub>3</sub> is aryl, substituted aryl, biaryl or heteroaryl other than imidazole, nitroimidazole and triazole;

each R is independently selected from the group consisting of -H, (C<sub>1</sub>-C<sub>6</sub>) alkyl, substituted (C<sub>1</sub>-C<sub>6</sub>) alkyl, (C<sub>1</sub>-C<sub>6</sub>) alkenyl, substituted (C<sub>1</sub>-C<sub>6</sub>) alkenyl (C<sub>1</sub>-C<sub>6</sub>) alkynyl, substituted (C<sub>1</sub>-C<sub>6</sub>) alkynyl, and (C<sub>1</sub>-C<sub>6</sub>) alkoxy;

the aryl substituents are each independently selected from the group consisting of -halo, trihalomethyl, -R, -R', -OR', -SR', NR'<sub>2</sub>, -NO<sub>2</sub>, -CN, -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR' and -C(S)SR';

the alkyl, alkenyl and alkynyl substituents are each independently selected from the group consisting of -halo, -R', -OR', -SR', NR'<sub>2</sub>, -NO<sub>2</sub>, -CN, -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR', aryl, γ-butyrolactonyl, pyrrolidiny and succinic anhydridyl; [and]

each R' is independently selected from the group consisting of -H, (C<sub>1</sub>-C<sub>6</sub>) alkyl, (C<sub>1</sub>-C<sub>6</sub>) alkenyl and (C<sub>1</sub>-C<sub>6</sub>) alkynyl, and

wherein thiophene is the only heterocyclic substituent.

6. (Amended) A method of treating an inflammatory disease, said method comprising the step of administering to a subject suffering from an inflammatory disease a therapeutically effective amount of a compound having the formula:



or a pharmaceutically acceptable salt or hydrate thereof, wherein:

n is 0, 1, 2, 3 or 4;

X is absent, (C<sub>1</sub>-C<sub>3</sub>) alkyl, (C<sub>1</sub>-C<sub>3</sub>) alkenyl, or (C<sub>1</sub>-C<sub>3</sub>) alkynyl;

Y is C, N, P, Si or Ge;

R<sub>1</sub> is absent, -halo, -R, -OR, -SR, -NR<sub>2</sub>, -ONR<sub>2</sub>, -NO<sub>2</sub>, -CN, -C(O)R, -C(S)R, -C(O)OR, -C(S)OR, -C(O)SR, -C(S)SR, -C(O)NR<sub>2</sub>, -C(S)NR<sub>2</sub>, -C(O)NR(OR), -C(S)NR(OR), -C(O)NR(SR), -C(S)NR(SR), -CH(CN)<sub>2</sub>, -CH[C(O)R]<sub>2</sub>, -CH[C(S)R]<sub>2</sub>, -CH[C(O)OR]<sub>2</sub>, -CH[C(S)OR]<sub>2</sub>, -CH[C(O)SR]<sub>2</sub>, -CH[C(S)SR]<sub>2</sub> or aryl;

Ar<sub>1</sub> is aryl, substituted aryl, heteroaryl other than imidazole, nitroimidazole and triazole, heteroarylium other than imidazolium, nitroimidazolium and triazolium, (C<sub>5</sub>-C<sub>8</sub>) cycloalkyl or (C<sub>5</sub>-C<sub>8</sub>) heterocycloalkyl;

Ar<sub>2</sub> is aryl or substituted aryl;

Ar<sub>3</sub> is aryl, substituted aryl, biaryl or heteroaryl other than imidazole, nitroimidazole and triazole;

each R is independently selected from the group consisting of -H, (C<sub>1</sub>-C<sub>6</sub>) alkyl, substituted (C<sub>1</sub>-C<sub>6</sub>) alkyl, (C<sub>1</sub>-C<sub>6</sub>) alkenyl, substituted (C<sub>1</sub>-C<sub>6</sub>) alkenyl (C<sub>1</sub>-C<sub>6</sub>) alkynyl, substituted (C<sub>1</sub>-C<sub>6</sub>) alkynyl, and (C<sub>1</sub>-C<sub>6</sub>) alkoxy;

the aryl substituents are each independently selected from the group consisting of -halo, trihalomethyl, -R, -R', -OR', -SR', NR'<sub>2</sub>, -NO<sub>2</sub>, -CN, -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR' and -C(S)SR';

the alkyl, alkenyl and alkynyl substituents are each independently selected from the group consisting of -halo, -R', -OR', -SR', NR'<sub>2</sub>, -NO<sub>2</sub>, -CN, -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR', aryl,  $\gamma$ -butyrolactonyl, pyrrolidinyl and succinic anhydridyl; [and]

each R' is independently selected from the group consisting of -H, (C<sub>1</sub>-C<sub>6</sub>) alkyl, (C<sub>1</sub>-C<sub>6</sub>) alkenyl and (C<sub>1</sub>-C<sub>6</sub>) alkynyl, and

wherein thiophene is the only heterocyclic substituent.